0050.1491-005 Docket No.:

Title: Genes Determining Cellular Sententers: Leonard P. Guarent cence...

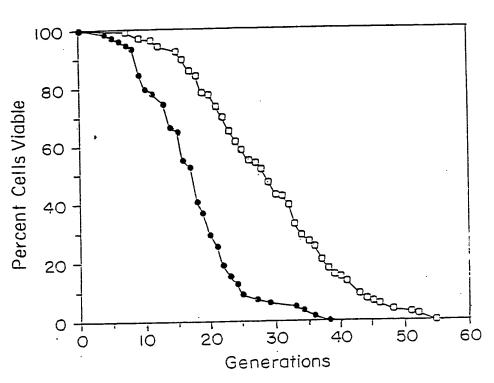


FIG. 1

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Sent Cellu

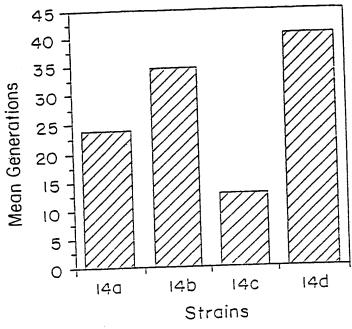


FIG. 2A

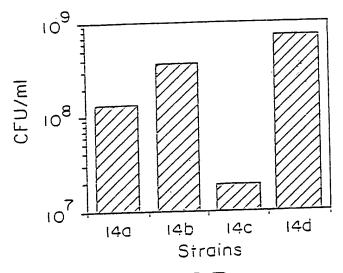


FIG. 2B

Title: Genes Determining Cellular Sene inventors: Leonard P. Guarente, e



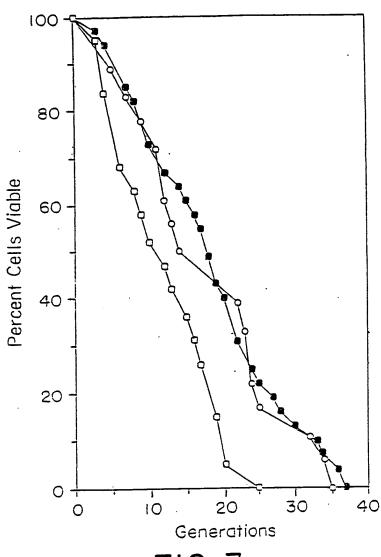


FIG. 3

0050.1491-005 Docket No.:

Title: Genes Determining Cellular Ser Leonard P. Guarente, Inventors:

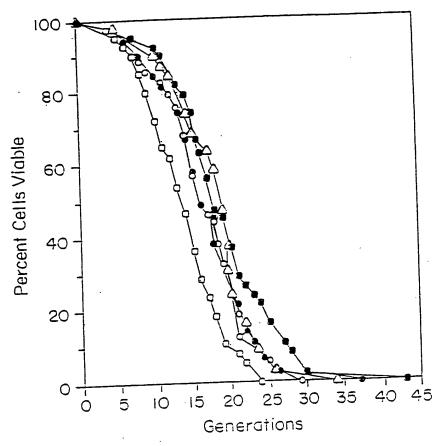


FIG. 4

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Sene nce.

Inventors: Leonard P. Guarente,

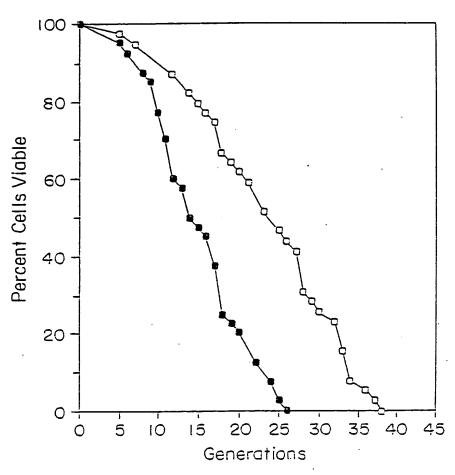


FIG. 5

ngspsyspinacia

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Ser Price Inventors: Leonard P. Guarente, al.

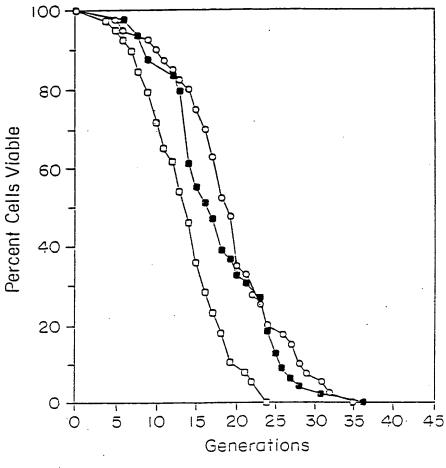


FIG. 6

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Ser

Leonard P. Guarente, Inventors:

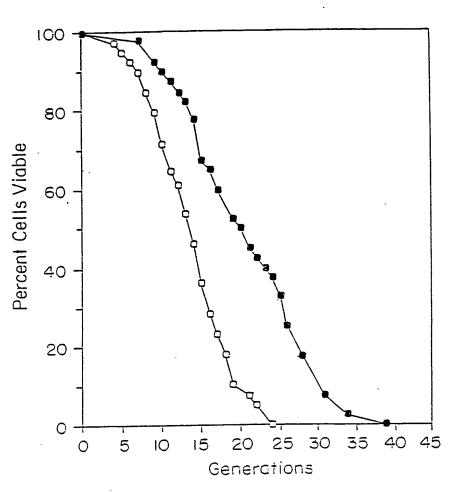
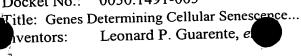


FIG. 7



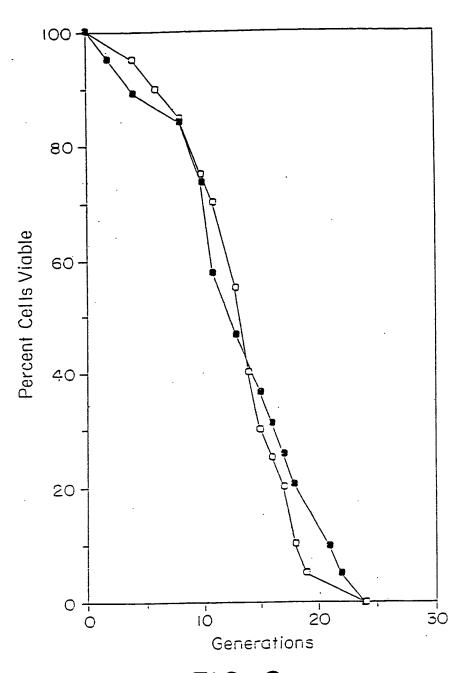


FIG. 8

0050.1491-005 Docket No.:

Title: Genes Determining Cellular So Inventors: Leonard P. Guarent cence...

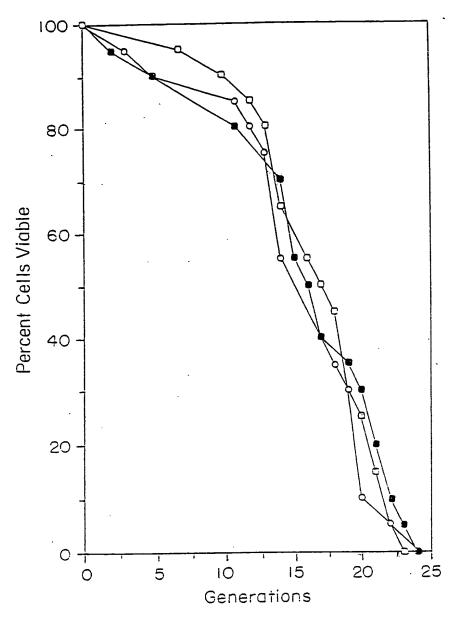


FIG. 9

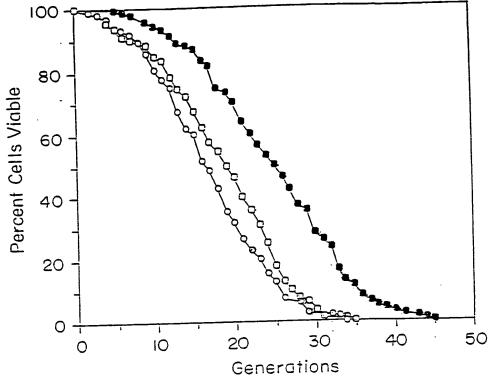


FIG. 10

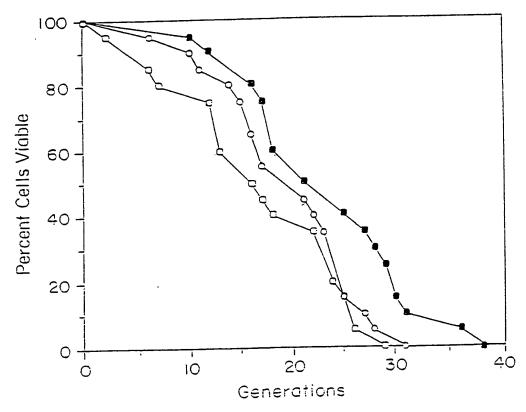


FIG. II

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarent al.

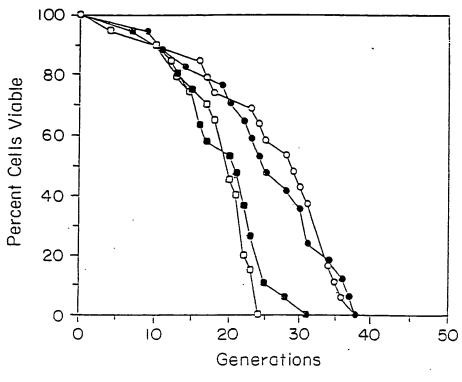


FIG. 12

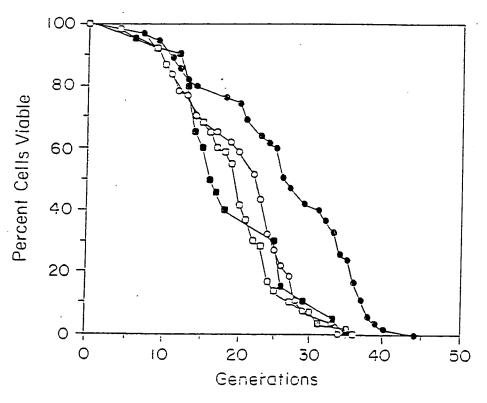


FIG. 13

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente

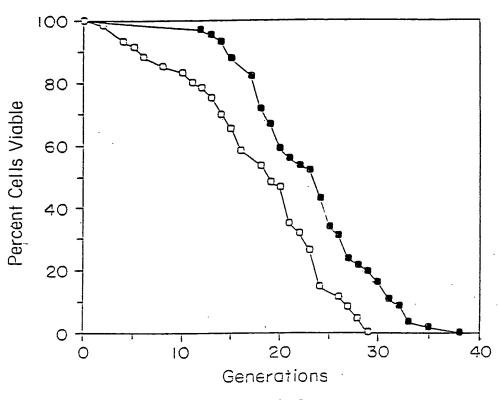


FIG. 14

Title: Genes Determining Cellular Senescence...
inventors: Leonard P. Guarente,

	-	_										
96	188	288	369 16	444	51.9 66	594 91	669 116	744	819 166	894 191	969	1044
TAG AATACACAGGGTGCCTAGTTCCTGGTGCCTGGATCTCGAGG	CCA TAA AAAGAA ATG TAG AGGTGGTGTTGACGTTTTGCCGC	GGCCCGGGTCGTGCGGAAAAAAAAAAAAAAAAAAAAAAA	ט	AAT N	CTA	CTA L	GAC	gcT A	GCC	TCT S	TT'A L	TGT C
rcrc	rt'ng	rttg	s AGC S	CAC	CAA	GCT A	AAC	ACC	GCC	GGT	TGG W	TAC
rggar	\CGT"	מככו	CTC	CCA (P	AAC (TCC (S	CAC 1	ACC 1	GCC (GTT (V	GAC 7 D	TAC Y
ומככו	TTG/	TTT	AAC K	CGA C	TAT A	TTA 1 L	CAC C	GCC 1	ACT (T	TCT (TTG (L	GGA 1
TGG	GGTC	TYTT	GCG TCT CCC AGA TCA AAG A S P R S K	GTA C	GAA 1 K	AAA 1 K	CAC C	GCT G	TCG 1	TCC 1	TCC 1 S I	GAC (
Trcc	AGG1	TTCC	AGA R	AAA G K	TTT G F K	ATG A	AAC N	CCA G	TCC T	TCT T S S	GTC T	CAA G
CTAG	TAG	ATT	CCC	AA A K	TTA T L F	AGT A	GAC A	ATT C	TTG T L S	TCT T	GCT G	TGT C
GTGC	ATG M	CAAA	TCT S	AAA AAA K	rtt t F	TCC A	AGT G	GTT A V	ACT T	TCC TS	GGT G	TCT T
CAGC	GAA	AAAA	GCG A	AAA A K	TCA T	AAT T N	CAT A	T.T G	ACT A	TCT T S S	CAA G	າ ເ
TACA	ANA	AGAC	TCG S	AAG A K	CAT T	AGA A R	CAC C	GCT GTT (ACC A T	TCC T S	GGA C	GCC ACC 7
G AA	TAA *	AAGC	ACC T	AAG AK	ATT C. I H	TCA A	GTC C	66C G	GCC A	TCC T	777 5 G	ACC G
T TA	CCA	AAAA	GAG K	ACT A	TTC A'	TTT T	C'F G	AC G	GCT G	TCT T	CCA T	AAC A
G TGT C	AGT S	AAAG,	CTT CTC GAG ACC TCG	GTA AC	TTA T' L	AAT T	CCA GCT	GCA GAC A D	GCT G	TCC T	TTC CO	GGT A
A ATG M	ATG M	GRAN	CTT L	TCG G	T'I'I' F	CTT A	GCT CO	AAC G	GTT G	TCT TO	GAT T	AAC G
TTTC	CCTA	rrgc.	TTC F	TCA TC	TAT TT Y	7700 CT 8 I.	GCC GC	GTC A	1'C'I' G' S V	TCC TC S S	rcr g s b	ATG AI
ນນນອ	AAAC	GTCC	TGT C	CTT TC L S	GT"I' T' <i>P</i> V Y	S CC TC	ö A	TAC GT Y V	GAG TC K S	77.00 77.0 S S	TGT TC	GAC AT
GGCCTAGGCCCTTCA	GATCGGGAAACCTA	ວຼວວວ	TA ATG TGT TTC M C F	CTC CT L		TTA CC	GTC TTG V L	CAG TP	GTC GA V K	TCT TC S S	rcc rc s	ATG GA M D
16660	'AGAT	נכפפכ	CTA		C TTC					T TC		C AT
CAGC	TTCC	ວວຍຍ	CCAT	T ACG	A AAC N	A AAT N	c gcc A	T ACT T	A AAG K	C TCT S	C ATT	c Arc I
ACGT	ı'cırı	GCAC	AATA	A TYYY F	C TTA	C AAA K	C ACC T	C GTT V	T GGA G	C GCC	T ACC T	GCT TCC A S
TGAAAAAGTGGAACTAGACCCCACGTCAGGG	CCGCGGCACTGGAAAAGCCCTTTTCTTTTCCA(TTTTGGGCAAGTAGGTCTTTCTGCACGGCCC	TCCTGATTCGGGTATATAAGTGAATACCATC	3 CAA	T TCC S	A AAC N	c TCC S	C ACC T	r gat D	c GCC A	r ggr g	6 GC
I'AGA	AAGC	3.rc.l.	rat'a.	A CCG	r CAT H	ו דדא ו,	A GCC	r Grc V	r GCT A	r gcc A	A GAT D	C TGG W
BAAC	SGAAJ	J'I'AGO	iGTA	. AAA K	ATT I	י מכיזי פ	TCA S	GTT. V	s GCT	rch S	r GAA K	2 6GC C
)GT/G(ACTO	CNAC	"rcac	TTT.	TPT.	7 CTT	r T'T'A L	, GCC	9 QCG	, ACC T	' 'r'r'' F	0 0 0
AAA	0000	7660	TGAT	GAT D	CAG CAG	GTC	GCT.	CGT R	TCG S	ACT.	GAT D	CT'A
TGA	ອວວ	TTT	J.J.C.C	AAA K	TTC	CTA 1.	'rra L	AAG K	ACC T	GC'I' A	GGA	GGT
e e	97	189	289 1	370	445	520 67	595 92	670	745 142	820 167	895 192	970 217

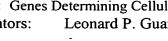
Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente,

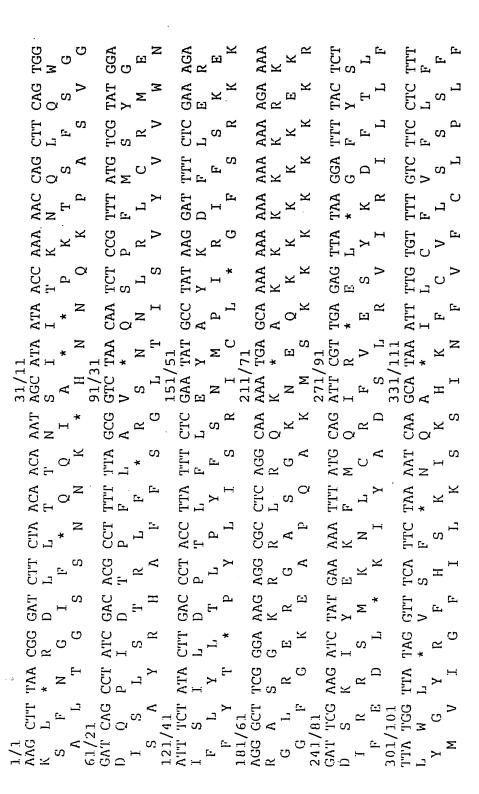
1119	11.94 291	1269 316	1344	1419 366	1494 391	1569 416	1644 441	1.734 451	1.809 24	1894 1	1946 17
GGT G	3 3 9	ATG M	TGG W	GGT G	TTIG L	ACC T	ÄCT	CAT	TAT Y		
GTT G	CAAG	AAC N	CAA 1	TGG G	TAC 1	TCT 1	GTT j	CGTT	TTT 7 F	ATG M	
TCC G	GGT C	GAA A K	TAT C	ATC T I W	ACT T	9667 T	TCA G	'ncτc	CCC T	ANA	
AGA T	GAA G K	TCT G S K	TAC T	TGT A	ATC A	GAT G	GTT T	GCC'IT'I'I'T'I'CCTTGAA'I'AT'I'GCAAATAAGCTTTTTGCTAGTACTTTT'I'I'I'I'TAC'I'CCGTTI'CAT	'AT C	atattatcatatagcatattatatagaaaaagtcaagaaaaaa	
GGT A	GTA G V K	GGT T G S	TCC T S Y	GGT T	GGT A	ACC G T D	ACT G T	CTTT	AAT ACA AAA AAA CAC AGT CCT TTG TAC TAT N T K K H S P L Y Y	TCAA	
GAT G D G	TGT G	CCA G	GAC T	GAT G D	GA'I' G D	GCC A	TGT A	AGT'A	TG T	aaag	
TCC GI	TTG TC L C	TAT CO	GAG GI K D	GAA GI K D	ACT G	GTT G	GGT T	rgcT	CT T	ATAA	
CCT TC	AGT TT	GAT TI	AAG GI K K	GTG GA V K	TAC AC	ATC G	GAC GO	TTT	ST CC	FAAC	
		c B	C AR	T GJ	TT T7			AAGC	S S	'ATA'	DD,
A CAA	T AAC N	r ACC T	c ATC I	c TCT S	r ggt g	C AAG K	C TCT S	AAAT	A CA	TAT	GAA TGA TTGC E *
r GAA K	2 ACT T	r ggt g	GTC V	r Grc V	r GCT A	2 ATC I	r GGC G	rrgc	A AA K	AGCA	4 TG
TCT S	: GAC D	TGT C	AAC N	rggT G	G GGT	' AAC N	rcr s	A'FA'	A A A K	\TAT!	GAI
CCT P	ACC	ATC I	ATC	GCT' A	TTG I,	TTT F	ე ენე -	TTG	ACP T	CATP	, TTC F
TGG W	AAC N	GCT A	CCA P	AAC N	GTC V	AAC N	TCT S	TTCC	AAT N	TTAT	CAT II
CAA Q	TCC S	ATT T	CAA Q	AAC	G'I'T V	CCA P	TAC Y	17171	CAC		TTG L
ACC T	CGT R	TCC S	TCC	G'F'T V	CCA P	GCA	GTC V	CCC	T"IC F	TAG *	T'TT F
AAG K	TAC Y	0 0	TCC S	TAC Y	GCC A	GAA K	GGT G	TAC TAG	T'T' F	CAC H	CTT L
		TCC S	GGT G	TAC	1'GG W	AAA K	AAT N	TAC Y	TCG S	T'AC Y	TAT Y
TAC Y	AAA K	GTC V	GCT A	CAA Q	AAC N	AAC	GAA K	TTC F	AGT S	NGA R	GCA
GG'T G	GGT G	AAG K	66C 6	GCC	GGT G	AAC N	TAC Y	GTC V	A'l'T I	T'TA L	ACT T
CCA P	AAC	AAC N	GTT V	TCT S	GTC V	CCA P		T'T'T F	TCA S	TTT F	ATA T
TCT S	AAG K		GTA V	ACC T	GGT G	AAC	TGC C	AAC	1'T'I' F	T'C'I' S	TCT S
TGT C	TGT C	GC'T A	ACC T	AAG K	TCC S	CCA P	GC'F A	GCT A	TAT Y	T'T'T F	CTT L
GCT A	TAC Y	CAA	CCT P	AAG K	GGT G	ATT I	GGT G	TCT S	GTT V	ATTT I	TCA S
	TTA L	GCT' ∧	G'I'T V	GGT G	GAG K	ATC I	AAT N	GGT G	ATG M	ATT I	TTA I,
	1.00 6	TCT	GTC V	C CAA	ACT:		GTC	17.T 2	LLL	TTC	7'''' F
1045 242	1.120 267	1195 292	1270 317	1345 342	1420 367	1,495 392	1570	1645 442	1735 1	1810	1.895 2

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guare





Docket No.: 0050.1491-005

Title: Genes Determining Cellular Segmence... Leonard P. Guarente

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FIG. 16C

Title: Genes Determining Cellular Senescence...

Leonard P. Guarent Inventors:

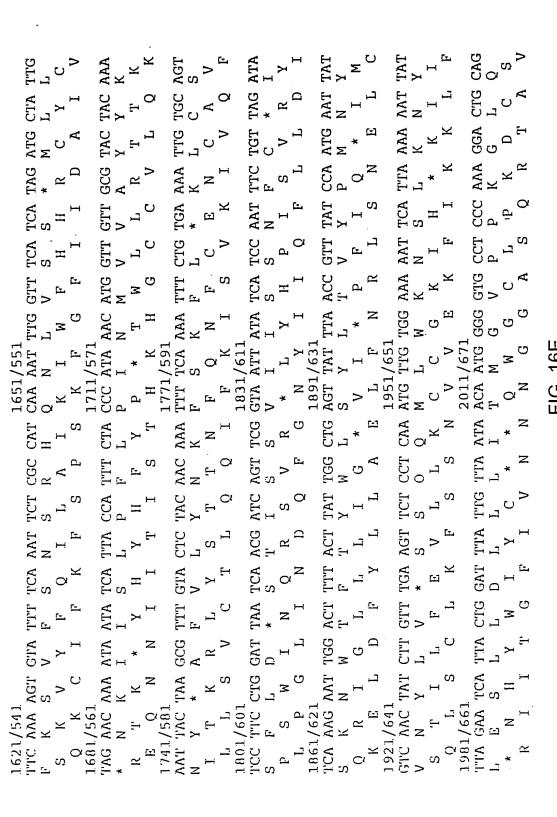
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S 11231 Y Y Y Y 1291 1291 1291 1291 1411 TTA GAG
L E
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AAA AAT
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A I
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B I
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ATA ACG

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guaren



I'I'G CT'T CTG ATG ACG TGA T'TA ATG CTT CTA

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarent

ATA ACA ATC TTC AAA CGA TTA ACA ACG AAA CAA AGA AAA ITA AGT IGA AAG TIA AAG CTT ATG CAG AAG CCA CAG GTA TAC CAT TCA CIK GGC AAA ACA GCT CTA GTA CAT TGA ATT ACG GTA ACT TTT GTA ACG ATT TTT CAT TGA AAA THE GTA ACT TEA THE TEE THA CAA AAG AAT TAE TTE CAA GTA TTA AAA CTA CAT EET ATG TAT TAG ACG TITA AGA ATT ATT CITC CITC TGC TITG CTT ACA ACA AAA ATA GTA ACG CAA TITG THA ATC TCC THA TCA GGG ATA ATT TTG GTA ATT ATG CGT TAC ANA CGC 2431/811 2311/771 2191/731 2251/751 ACA TAT CTC CTC AAG TCA CTG CAA TGA GTC × Ö ICA CAG TICA AITT œ 2341/781 2221/741 2281/761 2161/721

0050.1491-005 Docket No.:

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente,

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	ACA	<u>.</u>	0	, ×		ACA	H	0	N N N		GAA	F	×	×		TTC	Ē.	ß	=		CIL	1	ĬZ.	ß		ACA	:	0	, Z		TCI	S	בו	-
	ATA	<u>_</u>	*	Z		ATA	H	*	Z		ATA	H	*	~		AAA	×	z	H		CAC	=	H	д		TCG	ល	×			CGT	~	>	
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246	ATPA	<u>_</u>	- 4 c	×	252	CIK	-1	S	=	258	CTA	-1	*	z	264	CAC	=	H	O	270	CCL	24	-	വ	276	CGT	~	>	. —	282	CAC	=	Ţ	اخو

GAT TITA AGC AGC CTG GAT TTA TGA TGA ATG AAA CCG ACA AAA TTA ATG CTA ATC ACT TCT

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Leonard P. Guard Inventors:



AAT GIC AAG GCC CAT ATA ATC AAG TTA ATA TGA GCC GCA ACG CTA GTA TTT CCA ATA TGC CTG CCA THE TIT THE TITE OF THE THE THE THE ACA ANT ATT THA CGE AGA AAT CAA AGA CAA AAG AAA TGA ATA CCG CTA GAA CAT CTG ATG AAC TTC AAT TCA CTT TGC CAT AAT ACT TTT TTT TCT aat aaa aaa taa aaa ata aaa aat ica act aag caa iga cgt cct act aaa gic cca aaa ATC AAA CGG AAG GTG CAA ACT GGG ATT CAA GTT TGT CAA TGA AGT CGC AGC CGC CAT ACT CTA ATG CAA ATA GTC AAA ACT TCA ATG AAT CTT TTG TGC 3091/1031 3151/1051 3211/1071 3271/1091 3031/1011 2971/991 Oi ល U > Ö 3001/1001 3061/1021 3121/1041 3181/1061 3241/1081 2941/981

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I'I'I GAG CCG GAA AAA AAI GGI AAA GCA AAC I'AT I'GC CAI' C'I'I I'AT AI'I 1'I'G I'AI' I'CT GI'I'

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3301/1101

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guarer

THE GAA CAE GITA IVE AAA AIV CIVE CEA CIVG CET TIVG CAG GGT TAG CAT IVEC IVE CITA CEA AAA TGA TCT AAT TTT TTG AAT CGT TTT K * S N F F L N R F 3421/1141

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guar et al.

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0050.1491-005

Title: Genes Determining Cellular Senescence...

Leonard P. Guarente Inventors:

CAG Q R CCT GIT GAT ATT GIC CAC TAG TIC ICT TIT CAT ATT ITA ITT ICG CIT AIT TITE CCG THE THA CHG TITE CITE TOE CCT CGA AIT GTA ITT TAG ITT CCA ACG ITA GGA ITT C'I'N CAA AAG GTT TGA AAG AAG AAA TCG ATG ATG TAG TAG ACC CTG TCG TTT I. Q K V * K K K S M M Y II Q * T L S F GCT GTA ACA TIT TITA AGT GGA CCT ACG 571/191 691/231 631/211 C'I'I' CCG TAT ATT ACA TTG TAC ATT ATT TTT CI'TI TAG GI'TI CI'TI TITA AGA GIC I'CII GITI CATI THE CIT THE AGA ANG AGA GAR 601/201 661/221 541/181

TIGG AAC TAG ATG ATC CAG AGG AAA ACG CCA CCIT

AAA CAG TCA ATT CTG CTT TAG AGC AGT

0050.1491-005 Docket No.:

Title: Genes Determining Cellular Senescence... Inventors:

Leonard P. Guarente,

TAA ATG ACA ATT CAA TGA AGG TAT TGC CAA TCG CAT GGG CTG ATC ATA ATC CIT GIC CAT TITT THE CGC CCC CIG ATT THA CAG TGA ATG 961/321

TAT GGA CTC ATT CAA ACG TAC CAG GAT CAG CAT CTG TAG CCA TTG AAG AAA CCA CCG CTA

Docket No.: 0050.1491-005

CAA C'IG ACC ITA ICA ATG CGG CCA ACA ATG

Title: Genes Determining Cellular Se Inventors:

Leonard P. Guarente,

TITA ATA AAA CIIG CAC CAG CITA AAA AAG AGA GIIC CITA TOT TOT CAN AGG ACT TOO AAT CTG ACA TGC AGA ATT TTT CTA AGG CTA AGA AAC CGT TAG AAA CCT CGA AGG AGG ATT TGA Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Leonard P. Guarente Inventors:

TOO AOA TAT TAG CTO COO AGO AAA ACA COO COO CTO CTO COT TAA ACC CTA GIT CAA ATT CTG TTG CCT TTT CAG ATA TGA AGA ATG ATG GTG GTA AGC CCA CCG ATA ACG ACA AGG CGG GTC CAA ATG TTA GGA TGG ATT TAA TAA ATC CTA ATC GGG GAC CITY TAC TITC AAC CAA ATC CITA TITA TAA CCC AAT CGC CAA TTC ATC TTG CAC CTT TCT CTC CGA TTT CAA CIT ATG GTG CAG CAT ATC CAT ATG TAT CCT CCC CIT ATG AAA TGG GCG CGC AAT TTC AAC CAC TAA ATG CAA ATT CTC CAA TTC CTC S GGC CAT CAA TGC AAC CITY 1801/601 1981/661

2071/691

GGC TIT ATA GCA CIC CAC CIC CCT ICA ACG

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Leonard P. Guarer Inventors:

GCT ACT ATA ATA acc ant ata icg gaa gta tic act cat tst gta aag acc aac atg git gic git tic igc TI'S CGG ACG CAG T'IT CAA TGG TTC CGC CTC ATT TGT TGG TIG AGG AGT CGT CGA GAT GCG CCA ATA ATA AAC ATC I'G'I' CAA GIC ATA AIG ACA AIG ACA I'I'G GIA AI'I' CIA GIC GIT CTA ACG TIG GTA AAA TGA AAA ATA TGA AAA ACA ATA ACA ATA ATA ATA 2251/751 2131/71 2191/731 2311/77 2431/811 ACA GCG CGG AAA AAC AAC GTA AAA ACA ATA ATA ATA ATA ATA 2161/721 2221/741 2281/761 2341/781 2401/801 S

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Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente,

AAA AGC AGT 1GG ATA 1TC TCG GCA GTA AGG CGG CGG ACC GAA TTT TTG AAG AAA CTA AGG AGC CTG AAA ACT ATA GAC ACG TIC AAA AAT GIT TGC AAA GGT GGG CAT TAC AAA AAC CT"T TAC GCC 2491/831 2671/891 'FTG ACG CAA TCT CTG ATA GAA AGG ATT TAA ATG GTA ATC ATG AAG AGG TTA CCA CAG AAC AAA CAG ATG AAG AAG CAC AGA ICC AGIL TITA TCT 2641/881 2701/901 2761/921 2821/941

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senes

hventors: Leonard

Leonard P. Guarente,

ATT ACG TIT TAC AGA CAG CAT TAG ACA TIT CTC ATA AGC AAA ATG ACT ATC TCT ATA AAA GAC TAT CAG AGA TICC ACC TIGT TIGA AAC CAA GAG CCA TICG AAC TITT CTA TICC ATA AAT TITG GAT CAA ATG TIGA GGT GTT GCG TTT TGC AAC GTT GTC TAG ATC ATG GGA CTA CAG AAC AAT GTG ACA ATC TGT TAG CCC TITG ITG ATA AAT TAA CTT TGG ATC CAT TITG GCA ACT ATG IGC AAT ATA TAA TTA CCA AAG AGG CTG AGA AGA ACA AAT ATG ATT ATA CGC ATC GTG GCG AGA CGG GTA TTC AAT CAT TGT TGA ATG ATA GCT ACG GAA FIG AAA AAA TCT TGA AGA CAG CTA TIG TTT CGG AGC CAA TGA TTC 3151/1051 3091/1031 3241/1081 3061/1021 3001/1001

FIG. 17H

GAA ATA CAC CTC ATG GTA AAA GAA TCA TCG

3331/1111

I'NG TIGG CGC CITY TAC TIGG TIGG GCC CCA TAA

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarent

gia tac gtt taa cita tct gga taa acg tcg ctc cac agg ata ctg tag agg tcc tca aga CGC CCT AGA AAA CAG AAT GTT CTT ATT TAA ATA TAG GAA TIT ICA CIT TAT GGT ATA CIG GTA AAI TAA TAT CIT THE TAC AAT ACT TCA ANT GAA TAT CCA AAG CAA AAA AAA AGT GTT GAA GAA ATA AGA GAA GGA 3541/1181

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarent

ICA CCG TITA ITTA ACA AAT ITCA TCT AGT GTC CCC AAA ITTA AAA CTA GTT GCA GAA AAA TIIG ITA TTA GAT TGG ACT TGC GAA TTA TITT TGC CCA TITT GTT GGT TGC GCG TAA TCG GGA LITG I'I'T G'IG 1'I'C ATA AAT GGT ACT I'GT ACT GAA G'IG GGT ATT I'GC 1'GC 1'GA GCA T'IG AT'I GGT NIC ATA I'CA GAC ACG GAI' AAT' GAC CITA AAT' GAA GGC AA! ITA CHG THG THG THG THA ATA THG TTA ATA 3721/1241 3841/1281 3901/1301

Docket No.: 0050.1491-005

Title: Genes Determining Cellu

Title: Genes Determining Cellular Serscence...
Inventors: Leonard P. Guarent al.

, aac atc agg N I R act gaa gat cgg ggg gct gaa atc cat ctt cat cct acc gct ccg ccc gtg ttg gtg gaa tga cca gcc ctg tcc cag gat cta tag gag ttg cag gcc gtt ccc agg acg acg cta tgg P A L S Q D L * E L Q A V P R T · T L W agc agc ttg ggg gag gaa gtg gag S S L G E E E V E cay ggt cgc aag cgc agc cac aac cag ctg caa atc agg ctc ttg cag ctg gga ata aca tto atg. cag tgo ttt ggc agg act ctt tca oto and and can ota ato don aca tgo otg ttg ttt yct ata ata ata gca aac atc gat ggo cta ctg ggg 391/131 331/111 271/91 211/71 151/51 Cag act act tct ttc aga ggc agc atg gtg gog ttg cat gtg tot tga aga gaa aag a s 301/101 181/61 ಬ G

0050.1491-005 Docket No.:

Title: Genes Determining Cellular Senescence...

Leonard P. Guarente, e nventors:

att cag ttt cco ago caa tca tgg tgo aga gaa gao otg gto aga gtt tco atg tga ada I Q F P S Q S W C R E D L V R V S M * T yac caa aag gaa tat tcc tgg gtg atc aat ggc gag aca gtg cct ggg gaa cat cag atc D Q K E Y S W V I N G E T V P G E H Q I gtg agg tca att ctg tac tgt ccc cac gat cgg aga gtg ggg gac tag gcg tta gca tgg ttc aag cac ttg ctc tgg agg gaa gag cga tgg agt atg tgt tga gct cat ccc cgg gcg att cct gtc taa gaa aag gag gat ttg Ö Ö Ö 691/231 751/251 571/191 631/211 ~ Ö tgc gtt cca tgg atg aac tga atc atg att C V P W N N * I M I tgg gag age tet tge cag gta aaa agt ಭ Ö U 541/181

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Sen

Leonard P. Guarente, Inventors:

aaa aga aga aca agg gta cgt ttg yec aga act etg eta atg aag tgg ate tte tgg gte caa ace aga atg tac ctg tgg act cag cag caa ctg tgg tca aag att tta cca ago otg tgg agg cag acg ccc aga gty tcc cct tgg acc cca tgg caa ggg atg cag aca gtg atg aaa acg tac cag tgc aga atg gga att cag gca cgc agg cag ccc agc

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente,

ayy tto tco yty yay yay cca ycc aac yto ott tya ccc caa acc aga'acc ago ayy yao cty cay caa cta att cay cta atc aac aga cca cco cac agg ctc agc aag gac agc agc oty cyt tty toc cca atc cat aca tca tca gcy oty oto ccc cay gga cyg aco cot aca cag otg gat tgg ctg cag cag cga cac tag gcc cag ctg tgg toc oto acc agt att atg yay tta ctc cct yyg gag tct acc ctg cca gtc ttt tcc agc agc aag ctg ccg dtg ccg att ctc aac aac age tgt tec aaa gae eta atg ege ttg etg tee age agt tga eag etg ote age age age agt atg cae tgg cag etg ete ate age ege aca teg gtt tag 1471/491 1411/471 1531/511 1591/531 4 ß ø G ø Ü 1441/481 1381/461 1501/501 1561/521 တ ಭ

Title: Genes Determining Cellular Senescence...

nventors:

Leonard P. Guarente, &

ctg gtg ccc ttg tag tga atg cag gcg cga gaa atg gtc ttg gag ctc gtc gc ctg ttc gac ttg L V P L * * M Q A R E M V L E L L F D L W C P C S E C R R E K W S W S S C S T Ccca gtt ctt tct acg gca aca act ctc tga aca gca att cac aga gct ccc tct tct P V L S T A T T L * T A I H R A' A P S S ctt tag gaa cac agc ctc agc ccc agc ccc agc agc aca ata aca acc tgg 1, * E H S S L S P S P S S S P I T T W cat ttg cay oft cay caa atg gag cag ctg gtg gtg ttg ctg gaa caa caa atg Q L V V L L E Q Q M tay oto cty oco cay toa toa tta gtt cot cay oty cao aay cay oty cgg tgt tgg ctc R C W L ່ 1 1831/611 1951/651 2011/671 A A 1891/631 1651/551 o s ບ ctg ayd aaa cyg ato ccc tty tyg cag ß gtc tgg cag cag V W Q Q C C 1861/621 1981/661 1801/601 1921/641 _{ده} ح ß

-1G. 18E

Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guarente,

cct P agg.gac cag gac att cac aga cac cac ctt ctt R D Q D I H R H H L L ctg aag cca agt acc gca gtg caa gcg gcg I, K P S T A V O A A got taa aco tgg gag gad tca cga atg A * T W E D S R M 2371/791 2191/731 2251/751 2311/771 2131/711 tgo cto tco cta gto gat cct ctt caa yaa gat aca tct ctg ctg ctc cag CCB gtg act ccc ccc agg gct ctg ccc yac ccy tyg yca gea get tga eee gca gtg gct 2221/741 2281/761 2341/781 **4** 0 ø

Inventors:

Leonard P. Guarente,

gay god acy too tgt cat tgg cad tad aga tgt atg got god gtg tta tod aga aag otd acg tca ggt cca gat tca ttc agc tga aac tgg agc gtg cca cac cag ctg agc gcc agc ttg tct ctg gad ata taa tgg aat ttt ccc aag acc ago atg cca goo tot toa goo cya goa goa cto ttt tot ott cot otc gtt tgo gat atg gaa tgt ctt tgg cag aac gga att tto gaa aca aco I F E T T tto aga agt tot ttg aat ttg goa gto ttg aac aga agc tgg tca atg aaa tcc tcc agg ctg cct acc aac tca tgg tgg atg 2791/931 2731/911 2671/891 2491/831 cty aty tca tyo ctt cty yca gga yca ggd cca att tac aac tgc ggg aga ttg Ö 3 ල 2821/941 2701/901 2761/921 2641/881 2581/861

ttg agt tta ttc ctt cag acc agc aga atg aga tgg ttc ggg aac tag atg gcc atg tct

2911/971

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors:

age eee agt ett tge aat tta tea teg

3001/1001

Leonard P. Guarente

3061/1021 cac atc ctt atg gct gcc gag tga ttc aga gaa tcc tgg ago act gtc tcc ctg acc aga tga gtơ agc aca aat ttg' caa gca atg * V S T N L O A M cac tec eta tit tag agg age tie ace age aca eag age age tig tae agg ate aat tag cag aaa too gag goa atg tac ttg tat 3061/1021 3181/1061

0050.1491-005 Docket No.:

Title: Genes Determining Cellular Senemence...

Inventors:

Leonard P. Guarente,

ctg cgg ago cag gco ago gga aga tcg tca tgo R S Q A S G R S S C aga cgg tga agg acc agt atg tgg aga agt gtg tta ctc acg cct cac gta cgg agc gcg ctg tgc tca tcg atg agg tct gag gca gtg tca ccc got gtt ccc tca ttc ccg ctg cta gtg tag agt ctg 3331/1111 caa atc caa cca gca acc aga cca ago tgg aga agt act aca tga aga acg ggc ccc aca tcg caa ctc gee cae tgg

Title: Genes Determining Cellular Separcence...

Inventors: Leonard P. Guarente

agt ggt tgc tcc agg att act ccc tcc tcc aaa aaa gga atc aaa tcc acg agt gga aaa tga, bcc caa act 3931/1311 3991/1331 aca aac aaa aac aaa acc geo etg etg ttt tae tgg gco aca tat ttt 4021/1341

FIG. 18

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente

yta tit tot tgt tit gat gto taa tot gta tot ata aig tac oot agt 'agt oga aca tac aad tat ata tat ata tat aat gaa aaa ggt tto cgt att ttg agg atg gga ggg tgt gat tgt tta atg act act gga ttt ttt tat att att gaa agg taa aat ctg att att tag cat gag aaa aaa aat cca act ctg ctt ttg gad att aag ttt atg aaa ttd taa aaa atg cot gty tag act tty cat ata tac aaa ata tta tgo tga aga agg ctg tto gtg agg agg aga tgo gag I $_{
m L}$ C $_{
m K}$ R R $_{
m L}$ F V R R C E 1531/1511 4291/1431 ata tat agt gta tac ttg att taa cac tgt tta taa aaa ata tat ata aaa gct tca gtt tgt ttg ott cta aga gtt gct ttg gag act 4501/1501 4381/1461 4441/1401 4321/1441

Title: Genes Determining Cellular Senescence...

nventors:

Leonard P. Guarente, e

ict aaa tgi tat tca aga ttg agi ict cac tag tgi tti tit aat cci aaa aaa gia aig ttt tya tit igt gac agt caa aag gac gig caa aag tct agc ctt gcc cga gct tic cit tca acc aga agt aaa ttt ttt tgt ttt gaa gga ata aat gtt cit tat aca gcc tag tta atg ttt aaa aag aaa aaa ata gct tgg ttt tat ttg tca tct agt ctc aag tat agc gag att ott gta att ttt tya ttg tac aat tgt aca ttt gta tac ctg taa tgt aaa tgt gga gaa gtt ttt ggt aag aaa aga gaa tta goo ago oot gtg oat taa att 'tgt tgt ata ttg 4951/1651 4831/1611 att ctc acc ttt tat ggt cgt agc ata tag aac ata aac acg ttt 4681/1561 4741/1581 4861/1621 4921/1641

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarent

atg ctt atg cct ggg caa cta ttt tt gta act ctt gtg tag att gtc tct aaa caa tgt N L M P G Q L F F V T L V * I V S K Q C act cca atg aac ttt ttt gca ago aca ctt gta acc ata tgt gta taa tta aca aac otg tgt gtg aat cgc cct tcc ctt ttg tac aga aga igt ttg aat ata gaa ttg taa cac tac acg gtg tac att tcc aga gcc ttg tgt cat act 5011/1671 5071/1691 5191/1731 aca atc aga gcc cct ctc acc ttg taa agt gtg atc ttt att ttg aaa aat aca gaa ctt v I F I L K N T E L att ttg tct act tgt 4981/1661 5161/1721 5221/1741

FIG. 18M

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente

TAN GCA GCA NGG GGA CAA ATC ACC AAA GAA CAA GAA CIT TGA GAA AAG TAT CAC'AAA ACT TGG Ö K Ci GAA AAA GGG IGT AAA GCA GTT CAA GAA TGG ACC TAA AGT CAC ATC TAA AGA AGG T * R R F K E G K K V

FIG. 19A

Inventors:

Leonard P. Guarent

al.

TIGT TCG GGC AAA GCA GAT C S G K A D V R A K Q M CIT CAA AAA GAA GAA GAA AGA ACT GAA TGC ATT TGC ACA CGA TTC AAC C I C T R F N A F A H D S T AAA AAG AGT AAA GTT AAT K K S K V N K R V K I, M TGA CAA AGA A * Q R K D K E TAN AAC * The GCA GAA Git Gat ica agg gaa aat ${
m P}$ a E v d S R E N L I Q G K I AGC AGC CAA GAA GCC CAA ATG A ATC AC
I S
E S
N Q
361/121

COMPAND CONTRA

Inventors:

Title: Genes Determining Cellular Senescence... Leonard P. Guarent

TICA AGA ACA GAG AAA ACA GGC TITI TICA AGA CAA ATA TIC GAG AAA TAT TGT TAA GAA TGC AGA GAT AAT CAG AAG TTT C R D N Q K F GAT NCA GIG TTA CAT TOA GTA TGG ATT GCG AGA TIGA TITT GGT TIGA GITT ANG ATT TOT CAT GIA TGG AAG TAA ACC I S II V W K * T 661/221

19C

CGT GAG GAA GAT GCT GCG GCA TGC GGA AGC

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guaren

al.

ÇCC CCG CGA AGC GGT GGT CTA CCT GGC ACA CAC CAA AGC CAT TIT GGA GCA GAG GAA CAT GCT GAC GGA AGA GCT CTA TGG GAA CAC AFT TCA GAT IYOT AAC IYOC AAT GGC CCA AAA GGA AGC GGA CAA AST GIT AGA GGT ACA GCC AGA AAA AIT CIT GGA CIT ITT TAC CIA TGC ACC 961/321 TGT GAT TAA GCA CTC ATT GGT GCA TAA AGT ' D * A L I G A * S '' N K V ATT AGA ACT TAT TAT GGA TGA AAF GAA ACA I R T Y Y G \star N E T L I N D E N K Q CAA ACT CAG ATC AGA AAT GAT TGA AGC CAT AGC AGA TYCA CCG AAC TYCT SIC Cı GCT TTA CAA 1021/341 108/106

<u>nasere ounsil</u>

Title: Genes Determining Cellular Senescence...

Leonard P. Guarente,

nventors:

CCT AIT GTA CIT ACT AAG CCC CAG AGA TCC TGC ACA TAC: AGT ACG AGA AAT CAT TGA AGT TGA TGA TAC TAA GCT TGT GAA GCA GAT AAT GTG CCA TGG CAC GCC CAA GGA CAG GAA TEA AAA GET GEC TAA TGG CCA ATA CTC CAT AGT AAA TGA CAA ATA TGG AAG H S K * Q I W K ATT GCC TAG ACA CGA TGG CGC CAG AGT GGC CAT GCA CTG TTG TAT ACT GAT TGT GAA AAC AAT GAA GAC TYT GGT TYT ACT GGC GGC ATY TGA CAG TYC CAT ATC AGA AAT TAT 1261/42] 1201/401 1141/301

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Title: Genes Determining Cellular Senescence...

hventors:

Leonard P. Guarente, e

TOT GON ANA MGG AGA TGG AAA TGC ACA CAG TAA GAA MGA TAC AGA GGT CCG CAG ACG GGA CITY GGC NGC AND AGG ACT GCA TYCC TYGG TYGG GIC IGA CAT I'CT GGG AI'C I'GC CAC I'GG AGA ANG CTA CCT. GCA AGA ACA. CGC 1411/471 GGT CAG CGT TOA GCC TAC CAT GAA TGC CAT CGC GGT GCT AGA TAA GTC TGC GTG TGT GTT GCT CCT AGA AIC CAT TYC TYC AGG 1381/461 1501/501

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente

The totatic tricities certical respective and tricities and can assumed the range of the range ACT GAA AAG CTT GAT TCC TAC ACT GGA AAA AAC CAA AAG CAC CAG CAA AGG AAT AGA 'AAT T E K I, D S Y T G K N O K H O O R N R N TGG GAG NGA AGG TTG TTT TGC AAA AAC ACT THE THE MEG MEN THE THE GAN GIVE GIT TGC NOT AGA GOA NOT TWO TAT GAA GAA CCT GAA GTC CTG GGC TAG TGT AAA TCG AGG 1891/631 AAT AGA GCA NGA TAA AAA GAT GAA AGA AAA CAA GGA CGG NGA GCT TCA CAT TGC AGA ACA ಭ 1001/601 1061/621

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Inventors:

Leonard P. Guarente,

ATA GGT GGA AAG AGT TAA GAG CAA GAT GGA ATG ATT TTT AIT! GGG GI'A CIC I'CI' AI'A I'CI' GIT' 'I'CI' I'I'C I'AI' ACG AAI' CI'A I'I'' AI'A I'AA AIT 1951/651 TOT GIT! CIC 11ST ICT GIT! ICC CAA IGC TOT ACT TIGH AAA ACT GAG CAC S 2041/681 1981/661

FIG. 19

2101/701

0050.1491-005

Docket No.: Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente,

95	172 8	262 9	346 5	435	524 15	624	704 20	779 45	845 70	929 95	1004	1079 1456	1154	1229 195	1304
GGATCCCTCTGTGAGGCCGATT ATG CAG GCC TAG ACCCGCACGTGACCA CTTCGAGAGCAAGTTGCCTGCGAGTTTCTCTGCCCGAGGAAAAAAA 95	A ATG GAG GCA ATT TAC TTA ATA TGG TAT GAG AGG ATC TTT TGA CGGCAAATAG ATG CGC CAT CTC CGA GAA AAA ATC 172	CGAGCAAAAAATTTTTAAT ATG GGG TCA GTG GCG ATA TTA TAC TAT M G S V A I L Y Y	GGTGGTAGAATT ATG ATT GAA CTC CGA AAC TAA GCGCCGATT ATG GGT GGC AAA GCG		AGA TAC GAA TAT ACC TCA GTT AGT TTG TTT TAA CATTAAATATTCAACAGTTGCCAGTAGCAAAAAATATATCCATTCATT	TT""TCGTCTCATTACTGATATCCAACTAACAGTCTCCTTAGACGGTACCTTACTTTCCTTTTAAAATACTAGTATAGTCGCACATACTTAAAC 624	TCGTCTCTCTAACACATA ATG AAA ATT TCC GCA GCT TTA ATA TTG TCT TCC CTT TCT GTC GCA TTT TCT GCC CCT 704	GCA CCT GCT CCA GCG GAC AGT CAT GAA GAT CAT CAC AAA GAT GAA AAA CCA GCG GTT GTC ACT CAA 779 A P A P A D S H H E D H H K D E K P A V V T V T Q 45	TAC ATA GAT TCC AAT GCC GCT ACT AGT ACT GTA GGA TCT GCT ACT ACA TTG TCC TCA TCT GAG AAG 845 Y I D S N A A T S T' V E S A A T' T' T' T' T' T' S S E K 70	GAT ACC TCT GAA CAG AAG CGT GAT GGC GGA TTC CAA GAT GGT ACT GTC AAA TGT TCG GAC TTC CCT TCT GTA AAC 929 D T S E Q K R D G G F Q D G T V K C S D F P S V N 95	GGT NTA GTT TCC TTG GAC TGG CTA GGA TTT GGT GGA TGG GCC TCT GTC ATG GAC ATG GAT GCC AAC ACT TCG TCC 100	GAA TGT AAG GAT GGC TAC TGT TCT TAT GCA TGT GAA CCT GGA ATG TCA AAG ACT CAA TGG CCT TCT GAC CAA 107 E C K D G Y Y C S Y A C E P G M S K T Q W P S D Q 145	CCA AGC GAT GGT ART GGT GGT CTT TAT TGT AAA AAT GGT TAC TTG TAC CGT ACC AAC ACT GAT ACC AGC 115 P S D G K S V G G L Y C K N G Y L Y R T N T D T S 170	GAT TTA TGT TCT ACG GAT GAA ACA TCT GCT AAG GCC ATT AAC AAA AAG TCT GAC TCC ATT GCT CTA TGT AGG ACG 122 D L C S T D E T S A K A I N K K S D S I N A L C R T 195	GAT TAC CCA GGA TCT GAA AAC ATG GTG ATT CCC ACA GTG GTT GAT GGA GAT TCA CAA CCA ATT TCA GTC GTT 130 D Y P G S E N M V I P T V V D G G D S Q P I S V V 220
	96 .	173	263	347	436	525	625 1	705	780 46	855 71	930 96	1005	1080 146	1155	1230 196

1379 245	1454 270	1529 295	1604 320	1685 1	1760 26	1838 5	1913 30	1998 5	2072 23	2160 3	2245 15	2331 10	. 2406 35	2457 10
305 GAT GAA GAC ACT TAT TAT CAA 1GG CAG GGT AAA AAG ACT TCT GCT CAG TAC TAT ATT AAC AAC GCC GGT GTA TCT 221 D E D T Y Y Q W Q G K K T S A Q Y Y I N A A G V S	380 GCA GAA GAT GGG TGC ATT TGG GGT TCT GGT TCG GAT GTC GGC AAC TGG GCT CCA CTA GTG TTA GGT GCT GGT A	1455 TCC ACT AAT GGA GAA ACA TAC TTG TTG ATT CCA AAC CCC AAC AGT AAC CAA GCT GCC AAC TTT AAC GTT AAA 271 S T N G E T Y L S L I P N P N S N Q A A N F N V K	1530' ATA GIT GCA TCC GAT GGC GCT AAC GIT CAG GGC TGT GCG TAT GAA GAT GGC TCT TTC ACC GGA GAT GGT TCC 296 1 V A S D G A N V Q G S C A Y E D G S F T G D G S	1605 GAT GGT TGC ACA GTT TCT GTT TCT GGA TCT GCT GAA TTT GTT TTC TAT TAA GTCACTCTTTTTCGGTAAAAGA ATG 321 D G C T V S V L S G S A E F V F Y *	1686 "ICT TGT ATT TTG ATA CCC TCA ATT CCT ATT TTT CTT CCG CTC TCT ATT TAT TAT ACA TTG GGA 2 S C I L I P S I P L I I L F L P L S I Y Y Y T L G	1761 TTC CGT TAT ATT TTT CTC CTT TCA GTT CAT TTT ACT TCT TAA AAAGTTTCGTTGATCGCTATT ATG CTA TGG ATT CAA 27 F R Y I F L L S V H F T S *	1839 AGA TIT TCT TCT CTT CAA GGT GTA CTC TGC ATT ACG GTT TTC TTT AGT TCG TTT ATT TTT TTG TTA 6 R F S F L S L Q G V L C I T V F F S S F I F F L L	1914 ACA AGG TGT 1TG TAT ACA TAT ATA ATAT ATG GAA ATA 1TA TAG TGTTTATTTTGTTACTTCCTGCGAGTTGCAACAGAACTA 31 T R C L Y T Y I * M E I L *	1999 ACAAG ATG CCA TGC TGT TTT TCA TTT TTT GGC TAT AAA AAT AAC AGT ATC CTA GTC CTT GTG TTC GGC TTT 1 M P C C F F S F G Y K N N S I L V L V F G T	2073 AAA ATG GAA TG CAA ACC CCA TAA TTCCTTCTTCACACCAACAACCGCCTAGTAGTCGATTTTCAGAGACTCTA ATG CTT TGA ATA 24 K M B L Q T P *	2161 TAATTTTTTTTCTTCAAAATTTCCTTAAGCGTGCTATCGA ATG AGT AGA CAT CAA TCA AGA GTT TCA TGG TCT CCC CGT ATT TGC 1	2246 CGC TGC TTC TAA TATTTTGGAGTGTAGCCAATCAATCAATCAATCTTCGATA ATG CCA CTT TTT ACA TAT ACA CGA CAA 16 R C F *	2332 CCC ACA GTA GTA ACA CTC ATG ACT AAA TTT TCA TCA GTA CTT AAT GTC ATG TAA GGG GCT AAC GAA ATC AAT GCA 11 P T V V T L M T K F S S V L N V M L G A N E I N A	2407 ATG GGC GTT TCT CTA TAA ACG ATG ATA TGC GTA TTG TTC ACC ACT GGA TCC
13	13	14	15 2	16 3	16	17	38	19	19	20	21	22	23	24

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Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guaren al.

100	181	256 ⁻	331 69	406 3	501	589 9	664 34	739 59	814 84	889 109	964 134	1039 159	1114 184	11.89 209	1264 234
TGTTTAGFGCTACCCAACTACTTACATTCCTTTAAAAACCACAATATTTAAGTTAACCTGAGCTTTATTTTTTAGTAAGTTATTTACCACAATTTTTCTCA 1	TACACCTTTACAATCCGTATTGCC ATG AAT ACC AAG GCT TGC TCA GCT TCT GCA GTT CAA CCC TTT CCA ATA CCG CCA	ATG CGT CCT CAA AAC GTT AGT TTA GTC GTG CTC AAC CGC TAT TTT TGG TTT TAT CTT CGT TTC TTT CTG AAC	GAC ATT CGT CAC GAA AAT TTT CCT GAT GCG GAC ACT TTT TCC CGA TCC GGA CAT GCC TTT TTT D I R H E N C G G K F P D A D T F S R S G H A F F	TGG CGT TTC GCG TCA GTC AAT AGA AGT TTC AGA TCT ACA TTA GGA AGA ACC AGA AAA TAG CCATTA ATG CTT TCA W R F A S V N R S F R S T L G R T R K *	GCA TAG CACAGCATAGCAGCTGTGTATATCTTAAATAAG ATG TAG ACTGGTTTGGAAAGGTTTTGTGTAAGAAAAAAAAAA	AAAACAAGAGAAAAAAAAAAACACTTTACTAACTAATATCCTTTATTTTTT	T'TG AT'T AGT' T'C'I GGT GCC ATC GTG TCT TTA CCA CAC GTG GAT GTT CAC CAA GAA GAT GCC CAC CAA CAT AAG L I S S G A I V S A L P H V D V H Q E D A H Q H K	AGG GCC GTT GCG TAC AAA TAC GTT TAC GAA ACT GTT GTT GTC GAT TCT GAT GGC CAC ACT GTA ACT CCT GCT GCT R A A A A A A A A A A A A A A A A A A	TCA GAA GTC GCT ACT GCT ACT ATC ATT ACA ACA TCT GTG TTG GCT CCA ACC TCC GCA GCC GCT S E V A T A A T S A I I T T S V L A P T S S A A A	GGG ATA GCC GCT TCC ATT GCT GTT TCA TCT GCC TTA GCC AAG AAT GAG AAA ATC TCT GAT GCC GCT GCA TCT G I A A S I A V S S A A L A K N E K I S D A A A S	GCC ACT GCC TCA ACA TCT CAA GGG GCA TCC TCC TCC TCC TCG GCA ACT TCT ACC CTA GAA AGC AGC	TICT GIT TOT TOT TOT GAA GOT GOT COA ACA TOT ACT GTO GTG TOA ACT TOT GOA ACC CAA TOT AGT S V S S S S E E A A P T S T V V S T S S A T Q S S	GCT TCT TCT ACT ACT ACT TCT TCT ACT TCA CCA TCT ACT A	TCC TCT TCC TCC TCC TCC TCC TCT TCT TCT	GAC TIT TCA GGC CCA AGT GAG AAA GAC GGC ACT ATT CCA TGT GAC AAA TTC CCA TCT GGT CAA GGT GTC OD F S G Q G V
•-	101	182	25 <i>7</i> 45	332	407	502 1	590 10	665 35	740	815 85	890 110	965 135	1040	1115	1,190

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente,

			_								
1339 259	1414 284	1489 309	1564 334	1639 359	1714 384	1789 409	1864 434	1939 459	2022 476	2108 14	2150
TGC	TCT S	TTA L	TAC Y	CAA	GAA	ACT	GTT V	999 9	TTTTTT	CCT P	
TCA S	CCA P	TAC Y	GAC D	gac D	GTT V	TCC	ATA I	gAC D	TTT	CCA P	
GGT G	CAA	GAT D	ACC T			200 0		GCT A	CCTT	TGT	
၁၅၅	GAT D	GCG A	AGA R	GTT V	GTC V	GCT A	GTC V	ggT G	TAA GCTACGIGACTACTACTTTTCCTT *	TAC Y	
ACT				ACC T		GGT			CTAC	TTA L	
TCC		ACT (GCC (TAC		ACTA	TAT Y	
ACT T		AAC 1		CCA	AAC O				2010	CGA '	
GAC 1						TTA A			CTAC	TAC Y	
ACC C	ACC O			CT 1	TT!	CCA T	CA 1		AA G	TTT F	
AAC A	AAG A K		AAG G K		AC G	GCA C	AC G	AAT G N		TCT S	
GAA A	TCT A S K	TTG T L Y			AC T	TGG G W A	ac a	GAA A E		$ ext{TTT}$	
GTG G	ATG T M		CTA A			AAC T		TAC G		CCC P	ບ
GGT G	GGT A		AAA C K						GTC T	GTC V	TAT Y
TCC G S G	CCA G	AAT G N	TCT A S K	GTT G V E	TCT G	ATT G I G	CCA A	TGT G	TTC GF	ATG M	CAT
TGG T	CAA C	AAA AK	GTT T	TAT G' Y	ACA T	GGT A' G I		GAA TOE	CAT T		T'AC
GGA TC	TGC CL	TGT A	GTT G	ACC TY	AAG AC K T	TCT GC S G	CCT A	GGT G	GCT C	ATC	
GGT GC G G	TCC TC S								AAA GC K A	TCACACAATCACT	T'T'T (F
ဗ ဗ	ე 17C ა	3 TTG L	c TAT Y	c CCA	C AAA K	r gga g	3 ATT I	C ATC I			rg T
GA(TCC TAC	TT.	, GC(, ATC I	99 9	S S	TTG	· GTC	GGT	TAC	Α. A. M.
999	TCC S	ດີດີ	GCT A	GTT V	GAA E	AC'I	TCA S	NAT	TCC	CCTP	CCTC
ATT I	TGT C.	9 9 9	GAG E	ATG M	TGG ₩	GGT G	TTA L	TCC S	ACT T	יכככי	TGG
TGG W	TAC Y	GTC V	GTC V	AAC	ACT T	TGG W	TAC Y	TCA S	GTT V	CTC	TAA *
	TCC S	TCT S	GGT G	GAA E	TTT F	ATC I	ACA T	GAT D	TCT S	ACAT	CGT R
AT'T I	999 G	AGA R	T'GG W	ACT T	TAC Y	TGT C	3TG /	3AT	3TC /	GAAC	T'IT F
Trett S	GAG E	GGTľ G	GAA E	0 0 0	AC'F 'F	000 G	GGA G	r GCT C	ACC T	7.7.7.C	TCT S
ለፕፕ ነ	AAG K	GAC D	TGT C	CCG P		GAT	667 6	SCT A	TGT	CITTITITICGAACACATCTCACCCCCTATACC	TYPT TOT TYPT CGT TAA TGGCCTCA ATG
1265 235	1340 260	1415 285	1490 310	1565 335	1640 360	1715 385	1790	1865 435	1940 460	2023 1	2109 15

50 KKKKKKVRPH NFQCIHSLNF	100 ALILSSLSSV LLALS AVT.TLISSG	150 AVVIPAA HTVTPAASEV	200 AAATTSAAAS KISDAAASAT	250
	SRNSSMKLSA	TVTQYID TVTQYVNADG YETVVVDSDG	ATTTTL AATTTLSSTA VSSAALAKNE	EAAPTSTVVS
PQFTLLSSVT	VYFLETHSFL FEYNQLIVLP LNKNLPSLNF	EKPAVV DKRAVV .KRAVAYKYV -K-AVV	AATSTVES.A AADGKVESVA AAADSSASIA AAS-A	QDGTVKC EDGTISC ESSSVSSSSE
PRSKLSKDFK	FEYNQLLVLP	DSHHEDIHKD VHHSDNHHN VHQEDAHQH.	Tratisa Tsvlaptssa	TSEQKRDGGF SSSSVGSGDF SSSSSATSTL
1 MCFLLETSAS	S1 VYFLFIHSFL	101 AFSAPAPAPA ASTAVLAAPA AIVSALPHVD A	151 ATAATSAIIT	201 SSSEKD SSSSSSSSS ASTSQGASSS
Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus				

Title: Genes Determining Cellular Serescence...
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300SDFPSV NGIVSLDWLG FGGWASVMDM DANTSSECKDSDFPSG QGAVSLDWLG LGGWASIMDM NGNTATSCQD SATKSSTST SPSTSTST SSTSSSSSS SSSSSSNT DTSTGGSCKE	GYYCSYACEP GMSKTQWPSD QPSDGKSVGG LYCKNGYLYR TNTDTSDLCS GYYCSYACSP GYAKTQWPSE QPSDGRSVGG LYCKNGKLYR SNTDTNSLCV GSYCSYSCQP GMSKTQWPSD QPSDGRSVGG LLCKNGYLYR SNTDADYCLE G-YCSY-C-P GKTQWPS- QPSDG-SVGG L-CKNG-LYR -NTDLC-	TDETSAKAIN KKSDSIALCR TDYPGSENMV IPTVVDGGDS QPISVVDEDT EGOGSAOAVN KVSGSIAICG TDYPGSENMV VPTVVGAGSS QPINVIKEDS WGVEAAYVVS KLSKGVAICR TDYPGTENMV IPTYVEGGSS LPLTVVDODTA-C- TDYPG-ENMV -PT-VG-S -PVD-401	450 LVLGAGSTNG VVLGAGYTDG LNFGAASTGG
300 SDFPSV NGIVSLDWLG FGGWASVMDM DANTSSECKDSDFPSQ QGAVSLDWLG LGGWASIMDM NGNFATSCQD SATKSSTSST SPSTSTSTS SSTSSSSS SSSSSSNT DTSTGGSCKE	GYYCSYACEP GMSKTQWPSD QPSDGKSVGG LYCKNGYLYR TNTDTSDLCS GYYCSYACSP GYAKTQWPSE QPSDGRSVGG LYCKNGKLYR SNTDTNSLCV GSYCSYSCQP GMSKTQWPSD QPSDGRSVGG LLCKNGYLYR SNTDADYCLE G-YCSY-C-P GKTQWPS- QPSDG-SVGG L-CKNG-LYR -NTDLC-	TDETSAKAIN KKSDSIALCR TDYPGSENMU IPTVVDGGDS QPISVVDEDT EGOGSAOAVN KVSGSIAICG TDYPGSENMU VPTVVGAGSS QPINVIKEDS WGVEAAYVVS KLSKGVAICR TDYPGTENMU IPTYVEGGSS I.PLTVVDODTA-C- K-SA-C- TDYPG-ENMU -PT-VG-S -PVD-401	450 YYQWQGKKTS AQYYINNAGV SAEDGCIWGT SGSDVGNWAP LVLGAGSTNG YYQWQGKKTS AQYYVNNAGV SVEDGCIWGT EGSGVGNWAP VVLGAGYTDG YFTWEGKKTS AQYYVNNPGV SVEDGCIWGT SGSGIGNWAP LNFGAASTGG Y-W-GKKTS AQYYVNNPGV S-EDGCIWGT -GS-GNWAP L-GA-T-G
NGIVSLDWLG QGAVSLDWLG SSTSSSSSSS	QPSDGKSVGG QPSDGRSVGG QPSDGRSVGG QPSDG-SVGG	TDYPGSENMV TDYPGSENMV TDYPGTENMV TDYPG-ENMV	SAEDGCIWGT SVEDGCIWGT SVEDGCIWGT S-EDGCIWGT
SPSTSTSTST	GMSKTQWPSD GYAKTQWPSE GMSKTQWPSD GKTQWPS-	KKSDSTALCR KVSGSTAICG KLSKGVAICR K-SA-C-	AQYYINNAGV AQYYVNNAGV AQYYVNNPGV AQYY-NN-GV
SATKSSTST 	GYYCSYACEP GYYCSYACSP GSYCSYSCQP G-YCSY-C-P	351. TDETSAKAIN EGOGSAOAVN WGVEAAYVVS	YYQWQGKKTS YYQWQGKKTS YFTWEGKKTS YW-GKKTS
Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus	Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus	Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus	Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus

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- 00000	
500 SFTGDGSDGC VYSGSGSDGC EFSG.GADGC G-G-DGC SFSSGGSDGC	
VQGSCAYEDG VNGACSYENG VIGECVYENG V-G-C-YE-G VNGECIYENG	
451 ETYLSLIPNP NSNQAANFNV KIVASDG.AN VQGSCAYEDG SFTGDGSDGC ITYLSTIPNP NNKEAPNFNI KIVATDG.ST VNGACSYENG VYSGSGSDGC VTYLSLIPNP NNSDALNYNV KIVAADDSSN VIGECVYENG EFSG.GADGC -1YLS-IPNP NA-N-N- KIVA-D V-G-C-YE-GG-G-DGC -1YLS-IPNP NNGNALNFNV KIVAADDSST VNGECIYENG SFSSGGSDGC	
NSNQAANFNV NNKEAPNFNI NNSDALNYNV NA-N-N- NNGNALNFNV	515 FVFYZ FVFYZ FVLYN FV-Y-
451 ETYLSLIPNP ITYLSTIPNP VTYLSLIPNP -TYLS-IPNP	501 TVSVLSGSAE TVSVTSGSAN TVSVTSGKAH TVSV-SG-A-
Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sagl). Consensus	Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus Sun4

Title: Genes Determining Cellular Seinence Inventors: Leonard P. Guarente, al.

EIGHT REPEATS IN UTH4

193	LatDqFGcrFLQKkLE
231	LilDpFGnyLVdKicD
267	IsinqYGtrsLQKiID
310	LinDInGnhVIQKcIf
348	IstHkhGccVLQKiLs
384	LinDqFGnyIIQfiLD
422	LsclkFssnVVeKfIK
487	LirDnFGnyALQtlLD

HYDROPHOBIC CHARGED

FIG. 23

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Leonard P. Guarente, Inventors:

UTH4 YGL023 PUMILIO HUMAN	LatDqFGCRFLQKkLE LckDqHGCRFLQKqLD FsqDqHGSRFIQQkLE FsqDqHGSRFIQLkLE	i
·	Lil DpFGNYLIQKiCD Lmi DsFGNYLIQKiLE Lmi DvFGNYVIQKiFE Ľmr DvFGNYVIQKiFE	2
	IsiNqYGTRSLQKiID IslNpHGTRALQKlIE LalQmYGLRVIQKaLE LalQmYGLRVIQKaLE	3 -
	LinDlNGNHVIQKcIF LskDlNGNHVIQKcLQ CvkDqNGNHVVQKcIE CvkDqNGNHVVQKcIE	4
	IstHkHGCCVLQKLLS IdtHrHGCCVLQRcLD LstHpYGCRVIQRiLE LstHpYGCRVIQRiLE	5
	LinDqFGNYIIQFlLD LtlDpFGNYVVQYiIT LiqDqYGNYVIQHvLE LvqDqYGNYVIQHvLE	6
	LscikFSSNVVEKfiK LsiHkFGSNVIEKliK LsqHkFASNVVEKcVT VlsQhFASNVVEKcVT	7
	Lir DnFGNYALQT1LD LlnDsYGNYVLQTaLD MmkDqYANYVVQKmID MmkDqYANYVVQKmID	8

FIG. 24